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Note

Copper-catalyzed cyclization reaction: Unique synthesis of condensed thiazoles and selenazoles

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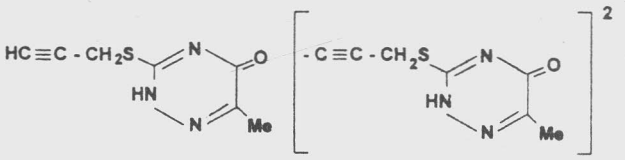
Synthesis of a variety of thiazolopyrimidines, thiazolo-1,2,4-triazines and selenazolo-1,2,4-triazines has been carried out by the catalytic action of Cu(II) salt on the corresponding propargylthio and propargylseleno derivatives..

Copper acetate has been reported to perfeorm oxidative coupling often called Cadiot-Chodkowicz and Eglington reaction[1-5]. Recently much attention has been paid to the acyclic and macrocyclic compounds constructed from diacetylenic fragments because of the interesting properties of diacetylenes[6-9].

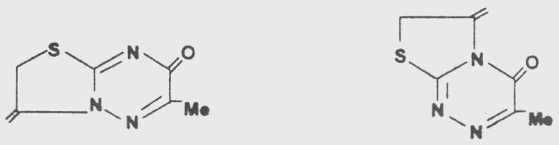
Diacetylenes are known to polymerize in the solid state by exposure to UV light, radiation or thermal annealing[10]. Very recently[11], oxidative coupling of bis - adenyl and bis-uracilyl diacetylene derivatives, obtained from the corresponding adenine-N(9) and uracil-N(1) propargyl derivatives, has been carried out using copper acetate.

To prepare the compounds containing two identical nucleobases connected by a tether with diacetylenic fragment, we chose as the first step, the preparation of 6-methyl-3-propargylthio-1,2,4-triazin-5(2*H*) - one **1**[12] and its conversion by oxidative coupling in the second step to the corresponding diacetylenic derivative **2**.

For the second step, we tried the classical Eglinton's method of oxidative coupling of acetylenic compounds using $Cu(OAc).H_2O$ in pyridine[13]. From this reaction two compounds were isolated. These compounds were identified as 2,3-dihydro-3-methylene-6-methyl-7*H*-thiazolo[3,2-*b*] [1,2,4]triazin-7-one **3** and 6,7-dihydro-6-methylene-



(1) (2)



(3) (4)

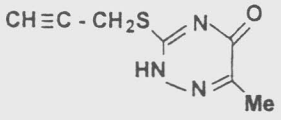
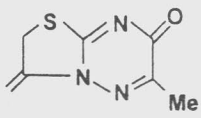
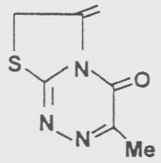
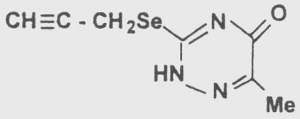
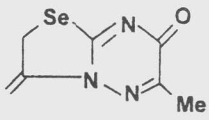
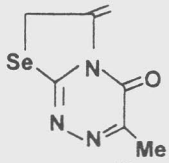
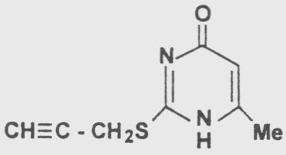
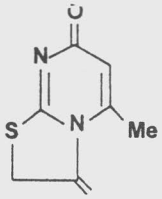
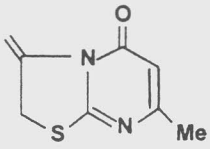
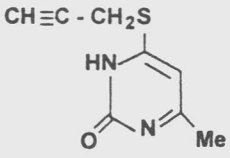
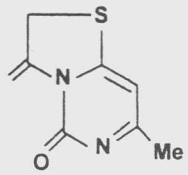
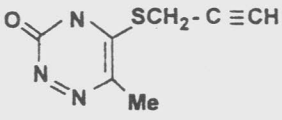
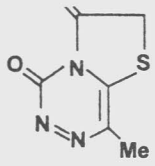
4*H*-thiazolo[2,3-*c*][1,2,4]triazin-4-one **4** in a fair ratio. This cyclization did not take place in the absence of the catalyst.

We have also made efforts to prepare a number of homocyclic and heterocyclic systems using base[12,14,15] and palladium catalyzed[16-22] intra-molecular functionalization of acetylenic moiety.

Although these cyclizations are fairly selective and give one regiosomer preferentialy, but suffer from two disadvantages. First, the Pd (II) salt catalyst, $(PhCN)_2PdCl_2$, is very expensive and secondly in the case of base catalysis, often more than stoichiometric amount of base such as MeO^-Na^+ and NaOH is required. Although copper acetate does not bring about a regioselective cyclization but it is an inexpensive material and provides the product in an excellent yield. To establish this methodology, cyclizations of other propargylthio (entries 3-5) and propargylseleno (entry 2) compounds were carried out using $Cu(OAc)_2$ as catalyst. Melting points, yields, propargyl compounds used and the products obtained are given in Table I.

In conclusion, it has been shown that $Cu(OAc)_2$ can catalyse the cyclization of propargylthio and propargylseleno compounds to the corresponding condensed thiazole and selenazole derivatives. Due to simplicity of the conditions, the above methodology should find utility in organic synthesis.

Table I — Catalyzed cyclization of propargylthio and propargylseleno compounds to condensed thiazoles and selenazoles using $Cu(OAc)_2$ as catalyst.

Entry	Substrate	Products	
		Based On 50% Theoretical Yield (Entries 1,2 and 3)	
1		 mp 180 - 181, lit[15] , 153 40%	 mp 105 - 106, lit[23] , 106 - 107 35%
2		 mp 189 - 190, lit[14] , 191 -192 35%	 mp 198 - 199 , lit[22] ,197 - 198 32%
3		 mp 192 - 193 , lit[24] , 190 42%	 mp 182 - 183 , lit[24] , 180-181 35%
4		 mp 198 lit[25] , 199 - 202 85%	
5		 mp 191 - 192 lit[20] ,190 - 192 80%	

Experimental Section

All products were identified by comparison with authentic samples (IR,NMR, mp).

General procedure. The appropriate propargylated compound (0.01 mole) and $Cu(OAC)_2$, H_2O (0.01 mole) were dissolved in MeCN(150 mL) and pyridine (10 mL) and the reaction mixture was refluxed for 5 hr and allowed to cool. The solvents were evaporated. To the residue water was added and organic materials were extracted with

chloroform. The chloroform extract was dried over $MgSO_4$ and the solvent evaporated to dryness. The crude product was subjected to column chromatography over silica gel using $CHCl_3$-MeOH(9:1) as eluent to obtain the corresponding cyclized products are major compounds. Their yields and mps are reported in Table I.

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